vitro dissolution study in three different solvents such as hydrochloric acid pH 1.5, artificial saliva pH 6.7 and saline phosphate buffer solution pH 7.4 respectively. And drug release from the *in vitro* dissolution study. **RESULTS:** The result reveals that prepared formulation F6 shown maximum value. The *ex vivo* permeation studies of Fluconazole drug through porcine buccal mucous membrane were performed and the results shown that F6 formulation was the best formulation among the prepared mouth dissolving tablets. **CONCLUSIONS:** Thus, the prepared (F6 formulation) mouth dissolving tablets had both local and systemic action and may be used for treating oropharyngeal and esophageal candidiasis (oral candidiasis) mainly as ulcer, burning sensation of buccal cavity particularly in premature infants, geriatric bed ridden patients, and patients with weak immune system caused by cancer treatment or diseases such as AIDS.

PCN44

TIME TO REIMBURSEMENT FOR ONCOLOGY AGENTS FROM EMA MARKETING AUTHORIZATION TO AIFA APPROVAL AS "C(NN)" CLASS VERSUS. AIFA APPROVAL AS "A" OR "H" CLASS

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OBJECTIVES: The purpose of this study was to evaluate the reduction in average market entry timelines for oncology agents in Italy if approved by AIFA as "C(nn)" class (non-negotiated class under the 189/2012 law) as compared to "A" (fully reimbursed) / "H" (hospital reimbursement). **METHODS:** For the purpose of this study, only the approval of the agents' first indications were taken into consideration. Included in this study were C(nn) oncology agents approved between May 27, 2013 and February 27, 2014 (aflibercept, pertuzumab, bosutinib, enzalutamide, vismodegib, pomalidomide, regorafenib, dabrafenib, infliximab, afatinib, radium Ra223 dichloride, trastuzumab emtansine) and class "A" / "H" agents approved between May 27, 2010 and December 2, 2013 (everolimus®, denosumab, pazopanib, cabazitaxel, denosumab, abiraterone, vemurafenib, vandetanib, axitinib). The average time to approval was calculated as the average difference between the date of issue of EMA marketing authorization and the determination date ("*determina*") in the Italian "*Gazzetta Ufficiale*". **RESULTS:** The average time to reimbursement for oncology agents from EMA marketing authorization to AIFA approval as "C(nn)" class was estimated as 111.3±39.9 days (n=12), while the average time to reimbursement as either "A" or "H" class was estimated as 428.3±109.0 days (n=9). This represents a significantly faster approval process (unpaired t-test, $p<0.01$), where on average, the C(nn) approval process is faster by 317 days. **CONCLUSIONS:** This study shows that time to reimbursement for oncology agents from EMA marketing authorization to AIFA approval is significantly expedited through the use of "C(nn)" classification, reducing market entry timelines by nearly a full year (317 days) compared to the regular "A" or "H" class approval process. Pharmaceutical companies seeking expeditious market entry into Italy for a newly approved oncology therapy targeting an area of high unmet need should therefore consider applying for C(nn) class.

PCN45

COVERAGE DECISION FRAMEWORK IN ASIA PACIFIC: A CASE STUDY OF TARGETED CANCER MEDICINES IN THE TREATMENT OF BREAST CANCER

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OBJECTIVES: To optimize access to cancer therapy in Asia Pacific (AP) nowadays became challenging due to budget constraints. Different decisions were made due to individual context, health care system and evidence required to support the decision. This study reviewed coverage decisions made by government in AP using targeted cancer medicines as a case study. **METHODS:** We selected 6 targeted cancer medicines recommended for breast cancer treatment based on the 2013 national comprehensive cancer network guidelines. Eight AP countries with different health coverage system were included to highlight the differences of health coverage system on decisions: four reimbursement countries [Australia (AUS), South Korea (KE), Taiwan (TW) and Japan (JP)] and four partial reimbursement countries [Malaysia (MY), Thailand (TH),China (CN) and Hong Kong (HK)]. We identified data from multiple sources including "Pubmed", government websites, payers and companies from inception till Jan 2014. We compared health coverage features, oncology coverage list and evidence requirement for decision making. Based on HTA approach, six possible supporting factors were compared. They included burden of disease, clinical effectiveness, economic evaluation (EE), budget impact analysis (BIA), public health impact, ethical concern and availability of alternative treatments. **RESULTS:** Efficacy and safety data were used as decision factors in all countries. AUS, KE, TW and TH considered both EE and BIA. AUS, KE and TH required local HTA evidence .Of six medicines, trastuzumab is now covered in most countries: AUS, MY, TW and KE. However, limited information is publicly available on evidence used in coverage decision in most countries except AUS where all factors except public health impact and ethical issue consideration are documented. **CONCLUSIONS:** Coverage decisions are affected by health care system and HTA evidence. Limited public documents related to coverage decisions are available. HTA system may lead to the development of explicit decision framework criteria for coverage decisions.

PCN46

THE INCIDENCE, PREVALENCE, AND SURVIVAL OF MALIGNANT MELANOMA IN TAIWAN

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OBJECTIVES: To understand the incidence, prevalence, and survival probability in the whole population in Taiwan. **METHODS:** This study utilized the 2005 to 2011 National Health Insurance (NHI) Research Database to study the disease. Inclusion criterion was that patients had at least two outpatient visits or one inpatient stay for melanoma (ICD9 code: 172). Patients' medical orders for outpatient visits and inpatient stay were linked. Their overall survival data were presented as product-limit survival probabilities. **RESULTS:** There were 240 to 290 new cases annually between 2006 and 2011. The raw incidence rate was about 1.1 to 1.26 per 100,000 persons,. The age adjusted incidence rate was around 1.5 per 100,000 persons. This was much lower than that the overall incidence in the US (21.1 per 100,000 per year). But it was similar to that of Asia-Pacific islanders in the US. The proportion of death between 2006 and 2011 were 28.8% and 21.9% among males and females respectively. This was different from the US population, whose 5 year survival was 91.3%. The population composition of the US was different from that in Taiwan and thus cannot be compared directly. About 29% of Taiwan patients were farmers. The mortality of farmers (36.5%) was slightly higher than that of non-farmers (22.4%). After controlling for age and sex, the hazard ratio of farmer vs. non-farmers was 1.136. Their age of diagnosis was much higher than the non-farmers: 82% and 34% for farmers and non-farmers diagnosed at age 65 and above, respectively. **CONCLUSIONS:** Malignant melanoma is found to be a rare but deadly disease in Taiwan. One reason for low survival probability was that farmers delayed the diagnosis to old age. It is suggested to screen farmers in early age.

PCN47

HOW SINGLE ARM PHASE II DATA CAN SUPPORT REIMBURSEMENT FOR ONCOLOGICS IN AUSTRALIA

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OBJECTIVES: The Food and Drug Administration (FDA) have approved 28 oncologics across 37 indications on the basis of pivotal Phase II data lacking an active comparator (Macaulay, ISPOR Toronto 2014). Approval was typically granted for indications with therapeutic alternative where a response rate ≥10% was demonstrated. This research aims to define the circumstances under which oncologics can obtain both regulatory approval and public reimbursement in Australia on this basis. **METHODS:** Public Summary Documents (PSDs) were extracted for any oncologic indication appraised by the FDA on pivotal Phase II data and the Therapeutic Goods Administration (TGA) and Pharmaceutical Benefits Advisory Committee (PBAC) decision and key rationale were extracted. **RESULTS:** 3 oncologics across 7 oncology indications (nilotinib in chronic myelogenous leukemia, dasatinib in acute lymphoblastic leukaemia (ALL), imatinib in ALL, dermatofibrosarcoma protuberans, myelodysplastic syndrome/ myeloproliferative disease and hypereosinophilic syndrome and/or chronic eosinophilic leukemia, and aggressive mastocytosis) have been granted TGA and PBAC approval on pivotal Phase II data. 2 were TGA approved but PBAC rejected (bevacizumab and cetuximab), 3 were submitted to PBAC on Phase III data, and no PSDs were extractable for the remaining 26 indications. In 7/7 approved indications, PBAC recognized active comparator alternatives. In 4/7, the rarity of these indications was cited as a key mitigating factor. For 2/7, overall survival (OS) data was presented that indicated potentially substantial OS benefits. In 1/7, a cost-minimisation argument was accepted against a recently approved comparator. Of the PBAC-rejected drugs, cetuximab raised key concerns over a lack of OS data, while significant trial comparability issues were expressed with bevacizumab. All PBAC-approved submissions included economic modelling on a cost/benefit, not cost/QALY, approach. **CONCLUSIONS:** PBAC can recommend the reimbursement of oncologics that offer potentially substantial clinical benefits based on an indirect comparison of single arms trials with acceptable cost-effectiveness as demonstrated on a cost-benefit metric.

PCN48

QUALITY CONTROL OF THE HUNGARIAN NATIONWIDE MAMMOGRAPHY SCREENING PROGRAMME

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OBJECTIVES: Organised, nationwide screening for breast cancer with mammography in the age group 45-65 years with 2 years screening interval started in Hungary in January 2002. According to the Hungarian guideline on mammography screening, an accredited mammography screening centre should perform 10000 examinations annually. The aim of this study is to analyze the quality control indicators of this screening programme. **METHODS:** The data derive from the financial database of the National Health Insurance Fund Administration (NHIFA) covering the period 2002-2010 year. We analysed 3 selected years: 2002, 2005 and 2010. The main indicator was the number of mammography screening examinations performed by the mammography screening centres. **RESULTS:** The annual number of mammography examinations was 323537 in 2002, 247045 in 2005 and 242601 in 2010. The number of accredited mammography screening centres were 51 (2002), 41 (2005) and 40 (2010). The average number of mammography examinations were 6344 (2002), 6025 (2005) and 6065 (2010) per year. In 2002, 14 mammography centres performed 10000 examinations in a range from 10314 to 25940. In 2005 only 4 mammography centres achieved more than 10000 examinations per year (range: 10294-17845). In 2010 again only 4 mammography centres achieved more than 10000 examinations per year (range: 10239-19259). **CONCLUSIONS:** Only a few number of mammography centres met the recommendation of the Hungarian mammography screening guideline and reached the target (10000 mammography examinations annually). Most of the mammography centres are not able to comply with professional guideline.

DIABETES/ENDOCRINE DISORDERS – Clinical Outcomes Studies

PDB1

INCRETIN THERAPY AND RISK OF PANCREATITIS IN TYPE 2 DIABETES MELLITUS: SYSTEMATIC REVIEW OF RANDOMIZED AND NON-RANDOMIZED STUDIES

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OBJECTIVES: To examine the association between incretin-based therapies and the risk of pancreatitis. **METHODS:** We searched Medline, Embase, CENTRAL and ClinicalTrials.gov to identify randomized controlled trials (RCTs), non-randomized clinical trials, cohort studies, and case-control studies of adults with type 2 diabetes mellitus that compared glucagon-like peptide-1 (GLP-1) receptor agonists or dipeptidyl peptidase-4 (DPP-4) inhibitors against placebo or active anti-diabetic medications. Trained reviewers, working in pairs, independently screened for eligible studies, assessed risk of bias, and extracted data. **RESULTS:** We included 59 studies (n=348,624), consisting of 55 RCTs (n=33,350) and 4 observational studies (n= 315,274). Pooled estimates of 55 RCTs (at low or moderate risk of bias involving 37 pancreatitis events, raw event rate 0.11%) did not suggest increased risk of pancreatitis between incretin agents versus control (Peto OR 1.11, 95% CI 0.57 to 2.17). Estimates by type of incretin agents suggested similar results (GLP-1 agonists vs. control: OR 1.05, 95% CI 0.37 to 2.94; DPP-4 inhibitors vs. control: OR 1.06, 95% CI 0.46 to 2.45). Three retrospective cohort studies (moderate to high risk of bias involving 1466 pancreatitis events, raw event rate 0.47%) also did not suggest increased risk of pancreatitis associated with either exenatide (adjusted OR 0.93, 95% CI 0.63 to 1.36 in one study, adjusted hazard ratio (HR) 0.9, 95% CI 0.6 to 1.5 in another) or sitagliptin (adjusted HR 1.0, 95% CI 0.7 to 1.3). However, a matched case-control study with moderate risk of bias suggested that the use of either sitagliptin or exenatide was associated with increased odds of acute pancreatitis (adjusted OR 2.07, 95% CI, 1.36 to 3.13). **CONCLUSIONS:** The available evidence suggests that the risk of pancreatitis in patients using incretin agents is very low, and does not support for the hypothesis that incretins increase the risk of pancreatitis.

PDB2

EVALUATING THE EFFECTS OF ANTI-THYROID DRUGS AND THYROIDECTOMY IN PATIENTS RECEIVING RADIOACTIVE IODINE THERAPY FOR GRAVES' HYPERTHYROIDISM - A RETROSPECTIVE STUDY FROM A UNIVERSITY TEACHING HOSPITAL IN SOUTH WEST, NIGERIA

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OBJECTIVES: This study evaluated the effect of anti-thyroid drugs and thyroidectomy on response of hyperthyroidism to fixed doses of Radioactive Iodine Therapy (RAI) and the incidence of hypothyroidism at 6months post RAI therapy. **METHODS:** A retrospective review of the medical records of 42 hyperthyroid patients treated with radioiodine to evaluate response rate of hyperthyroidism to two fixed dose regimens of 370 MBq (10 mCi) and 555 MBq (15 mCi) RAI therapy was carried out. The impacts of thyroidectomy and ant-thyroid drug pretreatment were documented. The treatment goal is to cure hyperthyroidism by rendering the patient either euthyroid or hypothyroid, within 6months of single dose of 370 MBq (10 mCi) or 555 MBq (15 mCi) RAI therapy. Statistical analysis was with SPSS version 15.0 and the level of statistical significance was taken as $P < 0.05$. **RESULTS:** The response (i.e. hypothyroid and euthyroid) at 6months post RAI for both doses of radioiodine was 71.4%, and after re-treatment of 7 patients who were earlier hyperthyroid after 6months, the response rate soared to 95.2%. The incidence of hypothyroidism (TSH > 6.1 mIU/L) was 47.6% with patients who had received 370 MBq (10 mCi) and 38.1% with those that received 555 MBq (15 mCi) radioiodine therapy. The use of anti-thyroid drugs (carbimazole or methimazole only) as pre-treatment increased response to RAI; Propylthiouracil however blocked response to RAI therapy in one patient Thyroidectomy, either total or subtotal, increased the response to RAI treatment. **CONCLUSIONS:** Radioactive iodine is highly effective for the treatment of Graves' hyperthyroidism, with a very high cure rate. Pretreatment with some anti-thyroid drugs protects against worsening of thyrotoxicosis after radioiodine and increases response to RAI therapy. Thyroidectomy increases the response to RAI treatment. However, the incidence of hypothyroidism should be anticipated and well prepared for as part of the treatment protocol.

PDB3

PREMIXED INSULIN LISPRO VERSUS INSULIN GLARGINE IN TYPE 2 DIABETES: A META-ANALYSIS

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OBJECTIVES: To systematically review the effectiveness and safety of premixed insulin lispro and insulin glargine in type 2 diabetes. **METHODS:** Such databases as PubMed, EMBASE, The Cochrane Library, ClinicalTrials.gov, CBM, CNKI and WanFang were searched for relevant studies from inception to October, 2013. Two reviewers independently screened studies according to exclusion and inclusion criteria, extracted data and assessed the methodological quality. Then, meta-analysis was performed using RevMan 5.2 software. **RESULTS:** 13 RCTs involving 4267 patients were included. The results of meta-analysis showed that, compared to insulin glargine, premixed insulin lispro effectively improved HbA1c levels [WMD=-0.18, 95%CI (-0.33, -0.02), P=0.03(parallel trials), WMD=-0.38,95%CI(-0.52,-0.24), P<0.00001 (cross-over trials)]. However, insulin glargine effectively improved FPG levels [WMD=0.82,95%CI(0.65, 0.99), P<0.00001 (parallel trials)]; WMD=0.64,95%CI(0.26, 1.02), P=0.0009 (cross-over trials)], weight gain[WMD=0.93, 95%CI(0.31,1.56), P=0.003 (parallel trials); WMD=0.74, 95%CI(0.19,1.29), P=0.009(cross-over trials)] and decrease hypoglycemia incidence[OR=1.26, 95%CI(1.10, 1.45), P=0,0007(parallel trials), OR=2.24, 95%CI(1.45, 3.46), P=0.0003(cross-over trials)]. **CONCLUSIONS:** : Premixed insulin lispro and insulin glargine have different advantages in clinical efficacy. Doctors should select the appropriate insulin treatment according to the patient's health condition and efficacy target.

PDB4

EFFICACY OF ADD – ON VILDAGLIPTIN THERAPY TO METFORMIN FOR TYPE II DIABETES MELLITUS PATIENTS IN SOUTH INDIAN RESOURCE LIMITED SETTINGS – PILOT STUDY

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OBJECTIVES: Prevalence of diabetes mellitus is increasing globally in most developed and developing countries and Dipeptidyl peptidase-4 inhibitors (Gliptins) are recently introduced class of drugs for type 2 diabetes mellitus which shows good glycemic control. It is a prospective interventional pilot study aimed to determine the efficacy of add-on vildagliptin therapy to metformin in type 2 diabetes mellitus patients for a period of 6 months in south Indian resource limited settings. **METHODS:** A total of 185 patients were enrolled into the study. The study subjects were assigned into three groups based on their existing treatment (initiated within one month) i.e., group I (vildagliptin and metformin), group II (vildagliptin alone) and group III (metformin alone). They were also assessed for baseline demographic characteristics. Medication adherence was measured to ensure that patients are complies with the treatment. The clinical endpoint was estimated by using various variables like quality of life and other clinical endpoints such as RBS, PPBS after three months of specific treatment through direct interview and by referring the medical case records. **RESULTS:** The results show that there is no significant difference in individual groups in terms of demographic characteristics. (P >0.01). And all the present study subjects are found to have more than 90 % of medication adherence. We observed high level of significant improvement in group I (93.18±3.76) subjects whereas low level of improvement in group III subjects (90.4±4.13) after the relevant treatment (P = 0.003). Group I subjects are also found to have good glycaemic control (RBS, FBS and PPBS) than any other treatment groups P<0.01). **CONCLUSIONS:** Add on vildagliptin therapy to metformin might improve the quality of life of type 2 diabetes mellitus patients and might be useful to bring the glycemic levels under control in type 2 diabetic patients in South Indian resource limited settings.

PDB5

DIAGNOSTIC TESTS OF BLOOD GLUCOSE: A SYSTEMATIC REVIEW

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OBJECTIVES: To evaluate the accuracy of different blood glucose determination methods, and provide a theoretical basis for governments to determine the mainstream glucose detection methods. **METHODS:** The MEDLINE, EMBASE, EBM REVIEWS, CBM, CNKI, Wanfang, Google academic search et al were were retrieved for literatures collection, literature quality evaluation was implemented by using QUADAS criteria, meta-analysis was carried out using Stata11.0 and heterogeneity test and sensitivity analysis was implemented. **RESULTS:** 20 studies were included, which contained a total of 2681 cases of patients. Meta analysis showed that values measured by the dry chemical method were significantly higher than glucose oxidase method, and no significant differences was found with the hexokinase method, no significant differences was yet found between the electrode method with enzyme method, the MD (95%CI) were 0.31 (0.09, 0.53), -0.51 (-0.14, 1.17) and -0.13, (-0.27, 0.02) respectively. Sensitivity analysis of the model, the sample source, research population, equipment and countries was carried out and conclusion was found no change between the methods. **CONCLUSIONS:** there was significant difference between different blood glucose detection methods; application of dry chemical measurement results should be cautious, we recommend using the glucose oxidase or diagnosis hexokinase method.

PDB6

EFFECTIVENESS OF HERBOTRIM AND MUNIPRABHA IN THE MANAGEMENT OF HYPOTHYRODISM

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OBJECTIVES: Hypothroidism is treated by replacement therapy of levothyroxine in allopathic system of medicine needs to be taken through out life time. In Ayurveda an ethnic system of Indian medicine has a remedy based on the drugs of natural origin which showes improved thyroid function. In this study the patients are treated for Hypothroidism with combination of two proprietary medicines (**Herbotrim and Muniprabha**) of Muniyal Ayurveda Pharmacy, Manipal. **METHODS:** Thirty cases Hypothyroidism are selected from Inpatients and Out patients of Muniyal Ayurveda Hospital, Manipal after obtaining the consent of the patients. The study was approved by intitutional ethics committe. The study design consited of observation before and after teatment with Herbotrim 2-0-2 (2 BID) with water and Muniprabha 1-1-1 (1TID) with water, tablets along with concomitant medicines for a period of 3 months. The subjective Obesity, Brady cardia, Somnolence, Slow mentationand objective criteria of assessment were T3, T4, TSH, Hb% and cholesterol. **RESULTS:** The Mean palsma T3 (mcg/dl) levels were 33.4 to 105.4, T4 (mcg/dl) levels were 2.38 to 11.36 and TSH (micro *IU*/ml) levels were109.4 to 6.63. The hemoglobin (g%) levels were increased from 10.05 to 12.24 and serum cholesterol (mg%) leveles were dropped from 280 to 158.9. **CONCLUSIONS:** Considerable improvement was observed in both subjective and objective criteria of assessment. There was decrease in subjective criteria like – Obesity, Brady cardia, Somnolence, Slow mentation, etc. There was increase in T3 and T4, and nd Hb%. The decrease in TSH and cholesterol with Herbotrim and Muniprabha in Hypothyroidism patients.

PDB7

DESIGN & METHODS FOR STUDY OF PREVALENCE, RISK FACTORS AND ECONOMIC BURDEN OF INSULIN INJECTION-RELATED LIPOHYPERTROPHY IN CHINA

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